UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,606	02/27/2004	Mary E. Brunkow	601117-109	9642

22504 7590 09/14/2005

DAVIS WRIGHT TREMAINE, LLP
2600 CENTURY SQUARE
1501 FOURTH AVENUE
SEATTLE, WA 98101-1688

EXAMINER	
XIE, XIAOZHEN	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 09/14/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/788,606	BRUNKOW ET AL.	
	Examiner	Art Unit	
	Xiaozhen Xie	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *88-100* is/are pending in the application.

4a) Of the above claim(s) *97-100* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *88-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *20040618,20041115*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1646, Examiner: Xiaozhen Xie.

The Information Disclosure Statement (IDS) filed 18 June 2004 and 15 November 2004 have been entered in full. Claims 88-100 are pending in this application. Claims 97-100 are withdrawn from consideration as being drawn to a non-elected invention. Claims 88-96 are under examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because: Non-initialed and/or dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c). Inventor David J. Galas made changes to his residence and P.O. Address without initializing and dating the changes.

Specification

The abstract of the disclosure is objected to because it does not describe the claimed invention. The abstract is directed to the TGF-β binding proteins,

whereas the instant disclosure is directed to the antibody, which binds to a TGF-β binding protein. Correction is required. See MPEP § 608.01(b).

Applicant is reminded of the proper content of an abstract of the disclosure.

A patent abstract is a concise statement of the technical disclosure of the patent and should include that which is new in the art to which the invention pertains. If the patent is of a basic nature, the entire technical disclosure may be new in the art, and the abstract should be directed to the entire disclosure. If the patent is in the nature of an improvement in an old apparatus, process, product, or composition, the abstract should include the technical disclosure of the improvement. In certain patents, particularly those for compounds and compositions, wherein the process for making and/or the use thereof are not obvious, the abstract should set forth a process for making and/or use thereof. If the new technical disclosure involves modifications or alternatives, the abstract should mention by way of example the preferred modification or alternative.

The abstract should not refer to purported merits or speculative applications of the invention and should not compare the invention with the prior art.

Where applicable, the abstract should include the following:
(1) if a machine or apparatus, its organization and operation;
(2) if an article, its method of making;
(3) if a chemical compound, its identity and use;
(4) if a mixture, its ingredients;
(5) if a process, the steps.

Extensive mechanical and design details of apparatus should not be given.

The use of the trademarks NP-40® (nonidet P-40) (claim 18 and pp. 5), HyBondN+ (pp. 78), Opti-MEM (pp. 81) and Lipofectin (pp. 81) have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to

prevent their use in any manner which might adversely affect their validity as trademarks.

"Nonidet P-40" is not a generic terminology. The U.S Patent 4,427,115 teaches the material sold under the name Nonidet P-40 (column 5, lines 55-58). The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 88-96 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent 6,803,453 B1.

An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim(s) because the examined claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985).

Here, claim 1-8 of U.S. Patent 6,803,453 B1 is drawn to an isolated antibody or antigen binding fragment thereof which specifically binds to a TGF-β binding protein selected from the group consisting of a polypeptide encoded by a polynucleotide that comprises SEQ ID Nos:1, 5, 9, 11, 13, and 15, or a complementary sequence. The antibody of the 6,803,453 B1 Patent differs from the antibody claimed in the instant application in that the instant antibody binds to a TGF-beta binding protein encoded by a polynucleotide which consists of SEQ ID Nos:1, 5, 9, 11, 13 and 15, and hybridizes under high stringency conditions to the complementary sequence or has at least 90% identity to a full length sequence. Although the conflicting claims are not identical, they are not

patentably distinct from each other because the instant claims are broader in scope, encompassing a genus of molecules related to the species claimed in the 6,803,453 B1 Patent. That is, claims 88-96 are anticipated by claims 1-8 of the 6,803,453 B1 Patent.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 88-96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody or antigen binding fragment thereof which specifically binds to a TGF-beta binding protein encoded by a polynucleotide that comprises SEQ ID Nos:1, 5, 9, 11, 13, and 15, does not reasonably provide enablement for an antibody to a protein variant encoded by a polynucleotide which: 1) hybridizes under stringent conditions to a complementary sequence of SEQ ID Nos:1, 5, 9, 11, 13, 15, or 2) has at least 90% identity to a full length sequence. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to an isolated antibody or antigen binding fragment thereof which specifically binds to a TGF-beta binding protein encoded by a polynucleotide having at least 90% identity to a full length sequence selected from SEQ ID Nos:1, 5, 9, 11, 13, and 15, or hybridizing under stringent

conditions to a complementary sequence thereto. The specification discloses antibodies for TGF-beta binding-protein of SEQ ID Nos:1, 5, 9, 11, 13, and 15. The specification further establishes that the antibodies have specific binding activity to TGF-binding protein. General guidance is given regarding how to make and test antibodies. The scope of patent protection sought by Applicant as defined by the claim fails to correlate reasonably with the scope of enabling disclosure set forth in the specification for the following reasons. The scope of the instant claims allow for amino acid substitutions in polypeptide by which the claimed antibody binds to. It is well known in the art that certain positions in a sequence are critical to the protein's structure/function relationship, such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. Particular regions may also be critical determinants of antigenicity, and these regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science, Vol.247, pp.1306-1310, especially pp.1306, column 2, paragraph 2). The Geysen et al. reference (J. Mol. Recognition, 1988, Vol.1, No.1, pp.32-41) teaches in a comprehensive study the replaceabilities of single amino acid in epitopes, which are specifically recognized by antibodies (pp.32, abstract). The Colman reference (Research in Immunology, 1994, Vol.145, pp.33-36) further establishes that single amino acid changes in antigen can abolish the antigen-antibody interaction entirely (pp.33, in particular). However, Applicant's specification has provided little or no guidance as to which amino acid sequences can be changed while maintaining the ability of the antibody to bind

TGF-binding protein. Since detailed information regarding the positions in the protein, which are tolerant to change, is lacking, it is unpredictable as to which encoding variations, if any, meet the limitations of the claims. Therefore, it would require the artisan to use the current invention as a starting point for further experimentation.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structure features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fails to recite any structural limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 88-96 are further rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 88-96 are drawn to a genus, i.e. antibodies to polypeptides encoded by polynucleotides of limited homology to SEQ ID Nos:1, 5, 9, 11, 13, 15. Applicant has disclosed one species, the antibodies to polypeptides encoded

by SEQ ID Nos:1, 5, 9, 11, 13, 15, but has not disclosed sufficient species for the genus as broadly claimed. A description of a genus of polypeptide sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structure features common to the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).* The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions, which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. A generic statement such as "an isolated antibody to a TGF-beta binding protein encoded by a polynucleotide that specifically hybridizes to a complementary sequence of SEQ ID Nos:1, 5, 9, 11, 13, 15, or that has at least 90% identity to the full length sequence" without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify polypeptides encompassed. One skilled in the art, therefore, cannot, as one can do with a fully described genus, recognize the

identity of the members of the genus. A definition by function does not suffice to define the genus because it is only an indication of what property the protein has, rather than what it is.

Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, the disclosure of SEQ ID Nos:1, 5, 9, 11, 13, 15 is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 88-96 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent 5,453,492. The 5,453,492 Patent teaches antibodies (monoclonal, polyclonal, or humanized) having specific reactivity with the TGF-β binding protein and hybridomas for producing an antibody (column 6, lines 62-67and column 7, lines 1-12). Although the 5,453,492 Patent is silent about the sequences of the TGF-β binding protein, it does not mean that the TGF-β binding protein does not possess the same or similar amino acid sequences as that recited in the instant claims. In other words, the recited amino acid sequences

are inherently present in the referenced TGF-β binding protein as they were obtained from the same source. Further, antibodies "cross-react" with antigens with homologous amino acid residues. Bost et al. (Immunological Investigations, 1988, Vol. 17, pp. 577-586) teach that antibodies which "cross-react" is due to the presence of a homologous sequence in each protein in which 4 of 6 residues were identical (see Abstract and Discussion). Even more, Bendayan et al. (J. Histochemistry and Cytochemistry, 1995, Vol. 43(9), pp. 881-886) teach that only a di-peptide is required for specific "cross-reactivity" between proteins.

Therefore, the reference teachings anticipate the claimed invention.

Conclusion

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Xiaozhen Xie, Ph.D whose telephone number is 571-272-5569. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Xiaozhen Xie, Ph.D
September 2, 2005

ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600